

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C. 20231  
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 11 February 2000 (11.02.00)	
<b>International application No.</b> PCT/US99/12298	<b>Applicant's or agent's file reference</b> 65937/6314
<b>International filing date</b> (day/month/year) 03 June 1999 (03.06.99)	<b>Priority date</b> (day/month/year) 04 June 1998 (04.06.98)
<b>Applicant</b> CHANG, Gwong-Jen, J.	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 04 January 2000 (04.01.00)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Antonia Muller Telephone No.: (41-22) 338.83.38
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## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

15

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 65937	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/12298	International filing date (day/month/year) 03/06/1999	Priority date (day/month/year) 04/06/1998
International Patent Classification (IPC) or national classification and IPC C12N15/40		
Applicant <del>THE GOVERNMENT OF THE UNITED STATES OF AMERICA</del> as		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  04/01/2000	Date of completion of this report  22.08.2000
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Chavanne, F  Telephone No. +49 89 2399 8399 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/12298

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-35 as originally filed

**Claims, No.:**

1-34 as originally filed

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**Drawings, sheets:**

1/8-8/8 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

- 
4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/12298

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims
	No: Claims 1-34
Inventive step (IS)	Yes: Claims
	No: Claims 1-34
Industrial applicability (IA)	Yes: Claims
	No: Claims 21-30

**2. Citations and explanations**

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**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

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**see separate sheet**

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following documents:

D1: Journal of Virology  
Vol. 72, No. 6, pp. 4925-4930, 1998

D2: Journal of Virology  
Vol. 72, No. 1, pp. 191-200, 1998

D3: Archives of Virology  
Vol. 141, pp. 743-749, 1996

2. D1 describes a DNA plasmid comprising a promoter derived from cytomegalovirus, which control the expression of the Japanese encephalitis virus premembrane (prM) and envelope (E) genes and a polyadenylation signal (abstract; page 4926, column 1, paragraph 1). D1 discloses the immunogenicity and protective efficacy of said plasmid DNA induced by a single immunisation, showing that its introduction into mice induced specific antibodies, CTLs and protective immunity (page 4928, column 2, paragraph 2, first sentence, paragraph 3, last sentence). The corresponding immunisation methods are also disclosed in D1 (page 4926, column 2). D1 also mentions the production of extracellular particles from cells infected with the plasmid carrying the prM and E genes (page 4929, column 1, paragraph 2). D1 also mentions DNA plasmids comprising the prM and E genes of the Saint Louis encephalitis, which induce partial protection in mice (page 4925, column 2, paragraph 2).  
Thus, in view of D1, the subject-matter of claims 1-34 is not novel. Therefore, considering the teaching of D1, claims 1-34 do not meet the requirements of Article 33(2) PCT.

3. D2 describes a DNA plasmid called pJME, which contains the coding sequences of both prM and E of the Japanese encephalitis virus and a poly-A terminator. Said prM and E genes are under the control of the promoter sequences of the immediate early gene of human cytomegalovirus (figure 1; page 192, column 2, paragraph 2). Cells transfected with this plasmid express the corresponding viral

proteins. E proteins were found in the lysate of said transfected cells. Secreted E proteins were also detected in the supernatant (page 194, column 1 to column 2, paragraph 1). D2 shows that mice immunised with said plasmid survive a lethal challenge (figure 3; Table 1). The corresponding method of immunisation and challenge is also disclosed in D2 (page 193, column 2, paragraph 1).

Thus, in view of D2, the subject-matter of claims 1-30 is not novel. Therefore, considering the teaching of D2, claims 1-30 do not meet the requirements of Article 33(2) PCT.

4. D3 describes a DNA plasmid expressing the Saint Louis encephalitis virus (SLEV) prM and E proteins under the control of the cytomegalovirus immediate-early promoter. This plasmid also comprises a poly-A terminator (abstract; page 744, paragraph 2). D3 mentions that cells transfected with said DNA plasmid express the prM and E proteins (page 744, paragraph 3). D3 further shows that a single injection with said plasmid achieved protection against SLEV (page 745, paragraph 3; figure 1).

Thus, in view of D3, the subject-matter of claims 1, 5-9, 13, 17-21 and 25-34 are not novel. Therefore, considering the teaching of D3, claims 1, 5-9, 13, 17-21 and 25-34 do not meet the requirements of Article 33(2) PCT.

## **VII. Certain defects in the international application**

1. Claim 31, 32, 33 and 34 referring to claims 1, 9, 13 and 21, respectively, it appears appropriate to move these claims closer to said claims 1, 9, 13 and 21.

## **VIII. Certain observations on the international application**

1. For the assessment of the present claims 21-30 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

# INTERNATIONAL SEARCH REPORT

International Classification No.

PCT/US 99/12298

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/40 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KONISHI E ET AL: "Induction of protective immunity against Japanese encephalitis in mice by immunization with a plasmid encoding Japanese encephalitis virus premembrane and envelope genes." JOURNAL OF VIROLOGY, (1998 JUN) 72 (6) 4925-30. , XP002119029 the whole document ----- -/-	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

15 October 1999

Date of mailing of the international search report

28/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Sitch, W

# INTERNATIONAL SEARCH REPORT

Inter. nat. Classification No.  
PCT/US 99/12298

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>LIN Y L (REPRINT) ET AL: "DNA immunization with Japanese encephalitis virus nonstructural protein NS1 elicits protective immunity in mice" JOURNAL OF VIROLOGY, (JAN 1998) VOL. 72, NO. 1, PP. 191-200. PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171. ISSN: 0022-538X., XP002119030 NATL DEF MED CTR, INST PREVENT MED, POB 90048-700, 18 SIH YUAN ST, TAIPEI 100, TAIWAN (Reprint); NATL DEF MED CTR, DEPT MICROBIOL &amp; IMMUNOL, TAIPEI 100, TAIWAN page 191 abstract</p>	1-30
X	<p>PHILLPOTTS R J ET AL: "Immunisation with DNA polynucleotides protects mice against lethal challenge with St. Louis encephalitis virus." ARCHIVES OF VIROLOGY, (1996) 141 (3-4) 743-9. , XP002119031 the whole document</p>	1, 5-9, 13, 17-21, 25-34
X	<p>VENUGOPAL K ET AL: "Immunity to St. Louis encephalitis virus by sequential immunization with recombinant vaccinia and baculovirus derived PrM/E proteins" VACCINE, vol. 13, no. 11, 1 January 1995 (1995-01-01), page 1000-1005 XP004057486 ISSN: 0264-410X the whole document</p>	1, 5-9, 13, 17-21, 25-34
X	<p>WO 92 03545 A (VIROGENETICS CORP) 5 March 1992 (1992-03-05) page 8, line 10 -page 9, line 14 page 52, line 30 -page 71, line 4</p>	1-30
X	<p>KOCHEL ET AL: "INOCULATION OF PLASMIDS EXPRESSING THE DENGUE-2 ENVELOPE GENE ELICIT NEUTRALIZING ANTIBODIES IN MICE" VACCINE, vol. 15, 1997, pages 547-552, XP002119032 cited in the application the whole document abstract</p>	1-30
X	<p>WO 90 01946 A (US GOVERNMENT) 8 March 1990 (1990-03-08) page 3, line 2 -page 10, line 30</p>	1-30
	-/--	



## SEARCH REPORT

PCT/US 99/12298

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE WPI  Section Ch, Week 199347  Derwent Publications Ltd., London, GB;  Class B04, AN 1993-373579  XP002119035  &amp; JP 05 276941 A (NIPPON ZEON KK),  26 October 1993 (1993-10-26)  abstract</p> <p style="text-align: center;">---</p>	<p>2,3,10,  11,14,  15,22,23</p>
A	<p>OSATOMI K ET AL: "COMPLETE NUCLEOTIDE  SEQUENCE OF DENGUE TYPE 3 VIRUS GENOME  RNA."  VIROLOGY, (1990) 176 (2), 643-647. ,  XP002119033  page 643  abstract</p> <p style="text-align: center;">---</p>	<p>2,10,14,  22</p>
A	<p>CHEN W ET AL: "Construction of intertypic  chimeric dengue viruses exhibiting type 3  antigenicity and neurovirulence for mice."  JOURNAL OF VIROLOGY, (1995 AUG) 69 (8)  5186-90. , XP002119034  page 5186  abstract</p> <p style="text-align: center;">-----</p>	<p>2,10,14,  22</p>

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/12298

## Box I Observations where certain claims were found uns archabl (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Remark: Although claims 21-30 and 34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATION SEARCH REPORT

information on patent family members

International Publication No

PCT/US 99/12298

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9203545 A	05-03-1992	US 5514375 A	07-05-1996
		AU 657711 B	23-03-1995
		AU 8728791 A	17-03-1992
		GB 2269820 A, B	23-02-1994
		JP 6503227 T	14-04-1994
		US 5744140 A	28-04-1998
		US 5744141 A	28-04-1996
WO 9001946 A	08-03-1990	AU 624863 B	25-06-1992
		AU 4206489 A	23-03-1990
		EP 0431064 A	12-06-1991
		JP 3503364 T	01-08-1991
JP 5276941 A	26-10-1993	NONE	

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>65937/6314</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 12298</b>	International filing date (day/month/year) <b>03/06/1999</b>	(Earliest) Priority Date (day/month/year) <b>04/06/1998</b>

Applicant

THE GOVERNMENT OF THE UNITED STATES OF AMERICA as

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.



the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing:



contained in the International application in written form.



filed together with the International application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.



Certain claims were found unsearchable (See Box I).

3.



Unity of invention is lacking (see Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/12298

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 21-30 and 34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/99/12298

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/40 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KONISHI E ET AL: "Induction of protective immunity against Japanese encephalitis in mice by immunization with a plasmid encoding Japanese encephalitis virus premembrane and envelope genes." JOURNAL OF VIROLOGY, (1998 JUN) 72 (6) 4925-30. , XP002119029 the whole document — —/—	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

15 October 1999

Date of mailing of the international search report

28/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Sitch, W

## INTERNATIONAL SEARCH REPORT

International Application No

PCT 99/12298

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIN Y L (REPRINT) ET AL: "DNA immunization with Japanese encephalitis virus nonstructural protein NS1 elicits protective immunity in mice" JOURNAL OF VIROLOGY, (JAN 1998) VOL. 72, NO. 1, PP. 191-200. PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171. ISSN: 0022-538X., XP002119030 NATL DEF MED CTR, INST PREVENT MED, POB 90048-700, 18 SIH YUAN ST, TAIPEI 100, TAIWAN (Reprint); NATL DEF MED CTR, DEPT MICROBIOL & IMMUNOL, TAIPEI 100, TAIWAN page 191 abstract	1-30
X	PHILLPOTTS R J ET AL: "Immunisation with DNA polynucleotides protects mice against lethal challenge with St. Louis encephalitis virus." ARCHIVES OF VIROLOGY, (1996) 141 (3-4) 743-9. , XP002119031 the whole document	1,5-9, 13, 17-21, 25-34
X	VENUGOPAL K ET AL: "Immunity to St. Louis encephalitis virus by sequential immunization with recombinant vaccinia and baculovirus derived PrM/E proteins" VACCINE, vol. 13, no. 11, 1 January 1995 (1995-01-01), page 1000-1005 XP004057486 ISSN: 0264-410X the whole document	1,5-9, 13, 17-21, 25-34
X	WO 92 03545 A (VIROGENETICS CORP) 5 March 1992 (1992-03-05) page 8, line 10 -page 9, line 14 page 52, line 30 -page 71, line 4	1-30
X	KOCHEL ET AL: "INOCULATION OF PLASMIDS EXPRESSING THE DENGUE-2 ENVELOPE GENE ELICIT NEUTRALIZING ANTIBODIES IN MICE" VACCINE, vol. 15, 1997, pages 547-552, XP002119032 cited in the application the whole document abstract	1-30
X	WO 90 01946 A (US GOVERNMENT) 8 March 1990 (1990-03-08) page 3, line 2 -page 10, line 30 -/-	1-30

PCT 99/12298

Relevant to claim No.	
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2, 3, 10,  
11, 14,  
15, 22, 23

2, 10, 14,  
22

$$\begin{array}{r} 2, 10, 14, \\ \hline 22 \end{array}$$



**INTERNATIONAL SEARCH REPORT**

Inform: patent family members

International Application No

PCT 99/12298

Patent document cited in search report		Publication dat	Patent family member(s)	Publication dat
WO 9203545	A	05-03-1992	US 5514375 A AU 657711 B AU 8728791 A GB 2269820 A,B JP 6503227 T US 5744140 A US 5744141 A	07-05-1996 23-03-1995 17-03-1992 23-02-1994 14-04-1994 28-04-1998 28-04-1996
WO 9001946	A	08-03-1990	AU 624863 B AU 4206489 A EP 0431064 A JP 3503364 T	25-06-1992 23-03-1990 12-06-1991 01-08-1991
JP 5276941	A	26-10-1993	NONE	

From the INTERNATIONAL SEARCHING AUTHORITY

RECEIVED  
EVEN & TABIN

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

To:  
FITCH, EVEN, TABIN &  
FLANNERY  
16th floor  
120 South LaSalle Street  
Chicago, IL 60603-3406  
UNITED STATES OF AMERICA

NOV 1 1999

Due 12/28/99  
pfjDate of mailing  
(day/month/year)

28/10/1999

Applicant's or agent's file reference

65937/6314

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 99/12298

International filing date  
(day/month/year)

03/06/1999

Applicant

THE GOVERNMENT OF THE UNITED STATES OF AMERICA as

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-(0) 340-2040, 1 x 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Barbara Klaver

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 45.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>65937/6314</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 12298</b>	International filing date (day/month/year) <b>03/06/1999</b>	(Earliest) Priority Date (day/month/year) <b>04/06/1998</b>
Applicant  <b>THE GOVERNMENT OF THE UNITED STATES OF AMERICA as</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 12298

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 21-30 and 34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Application No  
PCT/US 99/12298

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 C12N15/40 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KONISHI E ET AL: "Induction of protective immunity against Japanese encephalitis in mice by immunization with a plasmid encoding Japanese encephalitis virus premembrane and envelope genes." JOURNAL OF VIROLOGY, (1998 JUN) 72 (6) 4925-30. , XP002119029 the whole document --- -/--	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

15 October 1999

Date of mailing of the international search report

28/10/1999

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel: (+31-70) 340-2000, Fax: (+31-70) 340-3016

Authorized officer

Sitch, W

## INTERNATIONAL SEARCH REPORT

Application No

PCT/US 99/12298

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>LIN Y L (REPRINT) ET AL: "DNA immunization with Japanese encephalitis virus nonstructural protein NS1 elicits protective immunity in mice"</p> <p>JOURNAL OF VIROLOGY, (JAN 1998) VOL. 72, NO. 1, PP. 191-200. PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171. ISSN: 0022-538X., XP002119030</p> <p>NATL DEF MED CTR, INST PREVENT MED, POB 90048-700, 18 SIH YUAN ST, TAIPEI 100, TAIWAN (Reprint); NATL DEF MED CTR, DEPT MICROBIOL &amp; IMMUNOL, TAIPEI 100, TAIWAN</p> <p>page 191</p> <p>abstract</p> <p>---</p>	1-30
X	<p>PHILLPOTTS R J ET AL: "Immunisation with DNA polynucleotides protects mice against lethal challenge with St. Louis encephalitis virus."</p> <p>ARCHIVES OF VIROLOGY, (1996) 141 (3-4) 743-9. , XP002119031</p> <p>the whole document</p> <p>---</p>	1,5-9, 13, 17-21, 25-34
X	<p>VENUGOPAL K ET AL: "Immunity to St. Louis encephalitis virus by sequential immunization with recombinant vaccinia and baculovirus derived PrM/E proteins"</p> <p>VACCINE, vol. 13, no. 11, 1 January 1995 (1995-01-01), page 1000-1005 XP004057486</p> <p>ISSN: 0264-410X</p> <p>the whole document</p> <p>---</p>	1,5-9, 13, 17-21, 25-34
X	<p>WO 92 03545 A (VIROGENETICS CORP)</p> <p>5 March 1992 (1992-03-05)</p> <p>page 8, line 10 -page 9, line 14</p> <p>page 52, line 30 -page 71, line 4</p> <p>---</p>	1-30
X	<p>KOCHEL ET AL: "INOCULATION OF PLASMIDS EXPRESSING THE DENGUE-2 ENVELOPE GENE ELICIT NEUTRALIZING ANTIBODIES IN MICE"</p> <p>VACCINE, vol. 15, 1997, pages 547-552, XP002119032</p> <p>cited in the application</p> <p>the whole document</p> <p>abstract</p> <p>---</p>	1-30
X	<p>WO 90 01946 A (US GOVERNMENT)</p> <p>8 March 1990 (1990-03-08)</p> <p>page 3, line 2 -page 10, line 30</p> <p>---</p> <p>-/--</p>	1-30



Application No

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/12298

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9203545 A	05-03-1992	US 5514375 A AU 657711 B AU 8728791 A GB 2269820 A,B JP 6503227 T US 5744140 A US 5744141 A	07-05-1996 23-03-1995 17-03-1992 23-02-1994 14-04-1994 28-04-1998 28-04-1996
WO 9001946 A	08-03-1990	AU 624863 B AU 4206489 A EP 0431064 A JP 3503364 T	25-06-1992 23-03-1990 12-06-1991 01-08-1991
JP 5276941 A	26-10-1993	NONE	

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SAMPLES, K.H.  
FITCH, EVEN, TABIN &  
FLANNERY  
Suite 1600  
120 South LaSalle Street  
Chicago, IL 60603-3406  
ETATS-UNIS D'AMERIQUE

*pk*

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year) 22.08.2000

Applicant's or agent's file reference  
65937

**IMPORTANT NOTIFICATION**

International application No.  
PCT/US99/12298

International filing date (day/month/year)  
03/06/1999

Priority date (day/month/year)  
04/06/1998

Applicant  
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Vuilo, C

Tel. +49 89 2399-8061



# PATENT COOPERATION TREATY 09/701536

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 65937	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)																									
International application No. PCT/US99/12298	International filing date (day/month/year) 03/06/1999	Priority date (day/month/year) 04/06/1998																								
International Patent Classification (IPC) or national classification and IPC C12N15/40																										
Applicant THE GOVERNMENT OF THE UNITED STATES OF AMERICA as																										
1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.  2. This REPORT consists of a total of 5 sheets, including this cover sheet.  <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of      sheets.																										
3. This report contains indications relating to the following items: <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 5%;">I</td> <td style="width: 5%;"><input checked="" type="checkbox"/></td> <td>Basis of the report</td> </tr> <tr> <td>II</td> <td><input type="checkbox"/></td> <td>Priority</td> </tr> <tr> <td>III</td> <td><input type="checkbox"/></td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>IV</td> <td><input type="checkbox"/></td> <td>Lack of unity of invention</td> </tr> <tr> <td>V</td> <td><input checked="" type="checkbox"/></td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>VI</td> <td><input type="checkbox"/></td> <td>Certain documents cited</td> </tr> <tr> <td>VII</td> <td><input checked="" type="checkbox"/></td> <td>Certain defects in the international application</td> </tr> <tr> <td>VIII</td> <td><input checked="" type="checkbox"/></td> <td>Certain observations on the international application</td> </tr> </table>			I	<input checked="" type="checkbox"/>	Basis of the report	II	<input type="checkbox"/>	Priority	III	<input type="checkbox"/>	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	IV	<input type="checkbox"/>	Lack of unity of invention	V	<input checked="" type="checkbox"/>	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	VI	<input type="checkbox"/>	Certain documents cited	VII	<input checked="" type="checkbox"/>	Certain defects in the international application	VIII	<input checked="" type="checkbox"/>	Certain observations on the international application
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VIII	<input checked="" type="checkbox"/>	Certain observations on the international application																								
Date of submission of the demand  04/01/2000	Date of completion of this report  22.08.2000																									
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Chavanne, F  Telephone No. +49 89 2399 8399																									



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/12298

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-35 as originally filed

**Claims, No.:**

1-34 as originally filed

**Drawings, sheets:**

1/8-8/8 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/12298

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims
	No: Claims 1-34
Inventive step (IS)	Yes: Claims
	No: Claims 1-34
Industrial applicability (IA)	Yes: Claims
	No: Claims 21-30

---

**2. Citations and explanations**

**s e separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**s e separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

---

**see separate sheet**

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following documents:

D1: Journal of Virology  
Vol. 72, No. 6, pp. 4925-4930, 1998

D2: Journal of Virology  
~~Vol. 72, No. 1, pp. 191-200, 1998~~

D3: Archives of Virology  
Vol. 141, pp. 743-749, 1996

2. D1 describes a DNA plasmid comprising a promoter derived from cytomegalovirus, which control the expression of the Japanese encephalitis virus premembrane (prM) and envelope (E) genes and a polyadenylation signal (abstract; page 4926, column 1, paragraph 1). D1 discloses the immunogenicity and protective efficacy of said plasmid DNA induced by a single immunisation, showing that its introduction into mice induced specific antibodies, CTLs and protective immunity (page 4928, column 2, paragraph 2, first sentence, paragraph 3, last sentence). The corresponding immunisation methods are also disclosed in D1 (page 4926, column 2). D1 also mentions the production of extracellular particles from cells infected with the plasmid carrying the prM and E genes (page 4929, column 1, paragraph 2). D1 also mentions DNA plasmids comprising the prM and E genes of the Saint Louis encephalitis, which induce partial protection in mice (page 4925, column 2, paragraph 2).  
Thus, in view of D1, the subject-matter of claims 1-34 is not novel. Therefore, considering the teaching of D1, claims 1-34 do not meet the requirements of Article 33(2) PCT.

3. D2 describes a DNA plasmid called pJME, which contains the coding sequences of both prM and E of the Japanese encephalitis virus and a poly-A terminator. Said prM and E genes are under the control of the promoter sequences of the immediate early gene of human cytomegalovirus (figure 1; page 192, column 2, paragraph 2). Cells transfected with this plasmid express the corresponding viral

proteins. E proteins were found in the lysate of said transfected cells. Secreted E proteins were also detected in the supernatant (page 194, column 1 to column 2, paragraph 1). D2 shows that mice immunised with said plasmid survive a lethal challenge (figure 3; Table 1). The corresponding method of immunisation and challenge is also disclosed in D2 (page 193, column 2, paragraph 1).

Thus, in view of D2, the subject-matter of claims 1-30 is not novel. Therefore, considering the teaching of D2, claims 1-30 do not meet the requirements of Article 33(2) PCT.

----- 4. ----- ~~D3 describes a DNA plasmid expressing the Saint Louis encephalitis virus (SLEV)~~  
prM and E proteins under the control of the cytomegalovirus immediate early promoter. This plasmid also comprises a poly-A terminator (abstract; page 744, paragraph 2). D3 mentions that cells transfected with said DNA plasmid express the prM and E proteins (page 744, paragraph 3). D3 further shows that a single injection with said plasmid achieved protection against SLEV (page 745, paragraph 3; figure 1).

Thus, in view of D3, the subject-matter of claims 1, 5-9, 13, 17-21 and 25-34 are not novel. Therefore, considering the teaching of D3, claims 1, 5-9, 13, 17-21 and 25-34 do not meet the requirements of Article 33(2) PCT.

#### **VII. Certain defects in the international application**

1. Claim 31, 32, 33 and 34 referring to claims 1, 9, 13 and 21, respectively, it appears appropriate to move these claims closer to said claims 1, 9, 13 and 21.

#### **VIII. Certain observations on the international application**

1. For the assessment of the present claims 21-30 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.